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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/772,167	02/04/2004	Gregory E. Gonye	BC1042 US DIV	5571

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EXAMINER	
SHIBUYA, MARK LANCE	
ART UNIT	PAPER NUMBER
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,167	GONYE ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya, Ph.D.	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-22* is/are rejected.

7)☒ Claim(s) *22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/4/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 20-22 are pending.

Election/Restrictions

2. Applicant's election without traverse of the species of perturbing condition that is alterations in temperature in the Paper, filed 10/18/2006, is acknowledged.

Priority

3. This application, filed 2/4/2004, states that it is a divisional of 09/832,419, filed 4/11/2001, now US Patent No. 6,716,582, issued 4/11/2001, which claims benefit of 60/197,348, filed 4/14/2000.

Claim Objections

Claim 20 is objected to because of the following informalities: Claim 20 should probably state "the presence **of** other organisms" in line 5. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 20-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20, and its dependent claims, recites the limitation "a perturbing condition" in lines 12-13. There is uncertain antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Ashby et al., U.S. Patent No. 5,569,588 (IDS entered 2/4/2004).

The claims are drawn to a method for measuring gene expression responses to perturbation comprising: (a) constructing at least 2 identical cellular arrays, each cellular array comprising a reporter gene fusion comprising: 1) a reporter gene or reporter gene complex operably linked to 2) a genomic fragment from an organism of which at least 15% of the genomic nucleotide sequence is known; wherein at least one cellular array is a control array and at least one cellular array is an experimental array; (b) contacting the experimental array of (a) with a perturbing condition; (c) comparing the differences between the gene expression activity of the control and the experimental array wherein

gene expression response to a perturbing condition is determined; and variations thereof.

Ashby et al. throughout the patent and especially at the abstract, teach a method of detecting reporter gene product signals from each of a plurality of different, separately isolated cells of a target organism, wherein each of said cells contains a recombinant construct comprising a reporter gene operatively linked to a different endogenous transcriptional regulatory element (e.g. promoter) of said target organism such that said transcriptional regulatory element regulates the expression of said reporter gene, wherein said plurality of cells comprises an ensemble of the transcriptional regulatory elements of said organism sufficient to model the transcriptional responsiveness of said organism to a drug, contacting each said cell with a candidate drug, detecting reporter gene product signals from each of said cells before and after contacting each of said cells with said candidate drug to obtain a drug response profile, wherein said drug response profile provides an estimate of the physiological specificity or biological interactions of said candidate drug (column 1).

Ashby et al., at col. 6, line 50-col. 7, line 22, teach methods comprising genome reporter matrices comprising under one or more a variety of physical conditions, reading on perturbing conditions, such as temperature, reading on alterations in temperature, and pH, medium and osmolarity, (as in claim 22). Ashby et al., teach fusions as arrayed onto microtiter plates, reading on cellular arrays filed on a solid medium, or arrayed in liquid medium, as in claim 21. Ashby et al., state:

> Each of the cells contains a recombinant construct comprising a reporter gene operatively linked to a different endogenous transcriptional

> regulatory element of said target organism such that said transcriptional regulatory element regulates the expression of said reporter gene. A sufficient number of different recombinant cells are included to provide an ensemble of transcriptional regulatory elements of said organism sufficient to model the transcriptional responsiveness of said organism to a drug. In a preferred embodiment, the matrix is substantially comprehensive for the selected regulatory elements, e.g. essentially all of the gene promoters of the targeted organism are included. Other cis-acting or trans-acting transcription regulatory regions of the targeted organism can also be evaluated.

Ashby et al., at col. 6, lines 60-65.

Ashby et al., at col. 7, line 46-col. 8, line 13, teach determining a basal response profile for a genome reporter matrix, which is stored in computer memory. Response profiles for a stimulus are compared to the basal profile, thereby reading on methods comprising at least 2 identical cellular arrays.

This reference teaches an ensemble of reporting cells for use in the methods that comprises as comprehensive a collection of transcription regulatory genetic elements as is conveniently available for the targeted organism so as to most accurately model the systemic transcriptional response. Suitable ensembles generally comprise thousands of individually reporting elements; preferred ensembles are substantially comprehensive, i.e. provide a transcriptional response diversity comparable to that of the target organism. Generally, a substantially comprehensive ensemble requires transcription regulatory elements from at least a majority of the organism's genes, and preferably includes those of all or nearly all of the genes. We term such a substantially comprehensive ensemble a genome reporter matrix. It is frequently convenient to use an ensemble or genome reporter matrix derived from a lower eukaryote or common

animal model to obtain preliminary information on drug specificity in higher eukaryotes, such as humans (column 2).

Ashby et al teach an application of the genome reporter matrix in antibiotic and antifungal discovery. They teach that the genome reporter matrix offers a new tool to solve the problem of finding pharmaceutical targets in fungi that are specific to the fungus. Specifically, all molecules that fail to elicit any response in the Saccharomyces reporter are collected into a set, which by definition must be either inactive biologically or have a very high specificity. A reporter library is created from the targeted pathogen such as Cryptococcus, Candida, Aspergillus, Pneumocystis etc., i.e., fungi, (as in claim 9). All molecules from the set that do not affect Saccharomyces are tested on the pathogen, and any molecule that elicits an altered response profile in the pathogen in principle identifies a target that is pathogen-specific (column 5). This teaching reads on having assembled two genome-wide scale collections (because the reference teaches that these, which they call genome reporter matrix, are used in this particular method), perturbing each collection (both the Saccharomyces reporter collection and an additional fungus reporter collection) by adding the presence of a chemical (the elected species) to each collection. The response is measured from both reporter collections and analyzed to identify patterns of similarities and differences, as shown by the reference teaching that any molecule that elicits an altered response profile (which is a pattern of similarities when not altered, and a pattern of differences when altered) in the pathogen in principle identifies a target that is pathogen. Determination of altered response profiles between the two reporter collections determines (differences and

similarities of) gene function between the two organisms. Thus, the method steps of the claimed invention are taught by the cited reference.

This reference also teaches one embodiment of the method in which the reporter gene used is lacZ, (as in claim 12), and that a wide variety of reporters known in the art can be used, such as green fluorescent protein, lacZ, etc (column 7). The nucleotide sequence of Saccharomyces is over 50% known, (as in claim 13), because the whole genomic sequence is known in the art.

Furthermore, Ashby, at col. 6, lines 3-28), contemplate methods comprising a genome reporter matrix for organisms that are bacterial, as in claim 9).

The genome reporter matrix taught by Ashby et al reads on genome-registered collections because it is a set of strains containing reporter gene fusions to at least a majority of all known or predicted promoter regions. Although Ashby et al do not specifically indicate that the genome reporter matrix has been mapped by homology to the nucleic acid sequence of the genome of the organism, Ashby et al teach that the ensemble of strains is comprehensive (corresponding to a majority of the organism's genes, each of which is different from the others in the ensemble). "Mapping by homology" is merely acquiring homology information concerning the clones in the collection, which does not alter the structure of the collection, and thus a genome-registered collection has no structural difference from a collection that is not genome-registered. Accordingly, the genome reporter matrix taught by Ashby et al has the same structure as a genome-registered collection as claimed. And, because the same

method steps, using the same products, are taught by the cited reference, the teachings of Ashby et al anticipate the claimed invention.

8. Claims 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Larossa et al., U.S. Patent No. 6,025,131, (IDS entered 2/4/2004).

Larossa et al., U.S. Patent No. 6,025,131, throughout the patent and abstract, teach methods for identifying promoters, including e.g., at col. 11, line 20-col. 12, line 16, col. 14, lines 11-35, col. 16, line 45-col. 17, line 30, creating gene fusions where a regulatory region, responsive to some cellular stress, is fused to a luminescent reporter gene complex, wherein random fragments of genomic DNA are prepared by restriction digest or primer directed methods, (as in claim 5 and 6). Larossa et al., at col. 18, lines 26-38, disclose sequencing inserted DNA, to identify the inserted DNA in a plasmid. Larossa et al., at e.g., col. 10, lines 1-27, teach organisms that are enteric bacteria, (as in claim 9), including *Escherichia* and *Salmonella*, as in claim 11. Larossa et al., at col. 10, lines 34-55, teach reporter gene complexes that include *luxCDABE*, as in claim 12.

Larossa et al., at col. 1, lines 12-24, teach the synthesis of arrays of chemical compounds for screening. Larossa et al., at col. 3, line 64-15, teach methods for identifying regulatory regions modulated by a cellular insult, comprising creating a library of gene fusions in bacteria that are cultured in liquid media. Larossa et al., at col. 7, lines 44-56, col. 13, lines 22-50, teach cellular stress that includes physical treatments, such as changes in temperature. Larossa et al., at col. 13, line 50-col. 14,

line 10, teach growth of bacteria in a liquid medium, as in claim 21. Larossa et al., at col. 23, line 60-col. 26, line 2, teach methods of bioluminescent reporter detection by inducing stress in cells, including identification of regulatory regions responsive to dichlorophenoxyacetic acid on transformant-containing plasmid libraries grown in wells of a microtiter plate, and comparing light production in treated and untreated cultures, reading on at least 2 identical cellular arrays.

Conclusion

9. Claims 20-22 are rejected.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Shibuya, whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. James Schultz can be reached on (571) 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1639